

EDITORIAL COMMENT

Comorbidity and Outcome in Patients With Coronary Artery Disease*

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Most patients have more than one health condition, and therefore the assessment of comorbidity is important for patient care, for quality assurance, and for the evaluation of therapy. Comorbid diseases may affect multiple clinical outcomes, including mortality, functional capacity, quality of life, and cost. Clinical intuition tells us that diabetes, for example, has a strong effect on all of these outcomes and thus that the presence or absence of diabetes should be considered in the management of patients with coronary disease. Other comorbid conditions, such as chronic lung disease or renal insufficiency, probably have detrimental effects on outcome. Comorbid conditions in a patient with coronary disease may affect outcome directly or indirectly by reducing the patient's physiologic reserve and thereby increasing the risk of adverse outcome of coronary disease.

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Because comorbid conditions are important, how should their effect on outcome be gauged? One very easy way to measure the burden of comorbid conditions is simply to count them—how many problems are on the problem list? How many prescription medications does the patient take every day? A simple count of conditions or of pills would probably correlate with prognosis, quality of life, and cost. A simple count of conditions, however, implicitly assumes that outcome is equally affected by cancer as by hay fever, which seems implausible. A better method would be to construct an index that weighs comorbid conditions according to their impact on outcome so that cancer counts more heavily than hay fever. A properly weighted index would allow the effects of comorbid disease on outcome to be measured precisely.

The concept of a weighted score to gauge the burden of comorbid disease was applied to the prediction of mortality in a pioneering study by Charlson et al. (1). They empirically derived an index that predicted one-year mortality by studying 559 patients admitted to the general medical service of Cornell Hospital. They then tested the predictive power of their index in an independent cohort of 685 patients. The Charlson index assigns points to various

conditions, ranging from a weight of 1 for connective tissue disease to weights of 6 for metastatic solid tumor and for acquired immune deficiency syndrome; the sum of these points forms a global index of comorbidity. The Charlson index has been validated as a predictor of mortality in many settings since its original description in 1987 (2,3).

Despite the substantial track record of the Charlson index, there are both conceptual and practical limitations when applying it to patients with coronary artery disease (CAD). The Charlson index counts myocardial infarction and congestive heart failure as comorbid conditions. In a cohort of patients with coronary disease, myocardial infarction and heart failure are not really “comorbid” diseases but are actually complications of the underlying ischemic heart disease. Conceptually, these two conditions belong in a coronary disease severity index, not in a comorbidity index. At a practical level, the Charlson index was derived in a cohort of general medical patients, and the list of comorbid conditions and their weights may not be optimal for predicting the outcome of patients with CAD. The conceptual and practical limitations of the Charlson index suggest that a measure focused on patients with coronary disease might be worthwhile.

CAD-SPECIFIC INDEX

The study of Sachdev et al. (4) in this issue of the *Journal* modified the original Charlson index in two ways: 1) removing the coronary disease complications of myocardial infarction and heart failure; and 2) reweighing the remaining components of the index based on outcomes among 1,471 patients with documented CAD. The weights in their new CAD-specific index were derived from a multivariable Cox proportional hazards survival model analysis of 633 deaths observed over a mean follow-up of 13.6 years. The new CAD-specific index drops eight comorbid conditions from the original Charlson index, adds two conditions (current smoking, hypertension), and increases the weight given to four conditions (diabetes, chronic pulmonary disease, peripheral vascular disease, and renal disease).

Although confirmatory studies are needed to judge its value, the new CAD-specific index has considerable face validity. The database from which this index was derived was large, follow-up was lengthy and meticulous, and the number of deaths permitted analysis of the effect of multiple factors on mortality. The comorbid conditions in the index include most of the leading causes of death besides coronary disease: cancer, chronic respiratory disease, cerebrovascular disease, diabetes, dementia, and renal disease. Conditions included in the index are also recognized to increase the procedural risk of bypass surgery (5) and percutaneous coronary intervention (6). The CAD-specific index is likely to be a very useful measure in studies of mortality among patients with coronary disease.

The strength of the new CAD-specific index is that it

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was derived empirically from a large cohort of patients undergoing coronary angiography. This very strength, however, implies several important limitations. Comorbid conditions that are uncommon among patients undergoing coronary angiography are not included in the CAD-specific index. A relatively rare disease that carries a very poor prognosis (e.g., primary biliary cirrhosis, multiple sclerosis) is unlikely to have a sufficiently strong prognostic "signal" to reach statistical significance in an empirical study of patients with coronary disease. Most of the conditions that Sachdev et al. dropped from the comorbidity index were present in <2% of their patients. Furthermore, patients with advanced disease in other organ systems who were not candidates for aggressive treatment were probably not referred to coronary angiography. Thus, the CAD-specific index includes only the most common comorbid conditions that affect subsequent mortality.

The CAD-specific index was developed to predict mortality and therefore may not correlate as well with other outcomes. Osteoarthritis, for example, impairs functional capacity and increases medical costs. Osteoarthritis is a very common comorbid condition, yet it does not appear in the CAD-specific index because it has little, if any, effect on the risk of death. Although a comorbidity index may perform reasonably well in predicting outcomes other than death, its power to do so will likely be much less than in the predictor of mortality. The new CAD-specific comorbidity index is a

welcome development and highlights the importance of other diseases upon outcome in patients with coronary atherosclerosis.

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